

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of :
Hiroshi YANAGAWA et al. :
Serial No. [NEW] : **Attn: Application Branch**
Filed December 18, 2000 : **Attorney Docket No. 2000-1713**

LABELED PROTEIN AND ITS PRODUCING:
METHOD, LABELING COMPOUND TO BE
USED IN THE METHOD, AND METHOD :
FOR ANALYZING FUNCTION OF GENES
**(Rule 1.53(b) Divisional of Serial No.
09/190,276, Filed November 13, 1998)**

PRELIMINARY AMENDMENT

Assistant Commissioner for Patents
Washington, DC 20231

Sir:

In the interest of compact prosecution, please amend the present application as follows:

IN THE SPECIFICATION:

Page 1, between lines 3 and 4, add the following:

-- This is a divisional of Serial No. 09/190,276, filed November 13, 1998 --

Page 6, line 18, change "Fig. 4 is a photograph of electrophoretogram" to --Figs. 4A,
4B and 4C are photographs of electrophoretograms--; and
line 25, change "upper" to --Fig. 4A--.

Page 7, line 1, change "the middle" to --Fig. 4B is a photograph of an--;
line 2, change "illustrates" to --illustrating--;
line 5, change "The" to --Fig. 4C is a photograph--;

Page 7, line 6, delete "lower", and change "corresponds" to --corresponding--; and
line 7, change "CBB" to --CBB,--.

Page 12, line 12, change "I" to --V--;
line 13, change "II" to --VI--.

Page 16, line 3, change "I" to --V-- and change "II" to --VI--.

Page 27, line 2 from the bottom, change "Fig. 4 shows" to --Figs. 4A, 4B and 4C
show--.

Page 28, line 4, delete "the";
line 5, delete "upper and middle electrophoretograms in", and change "Fig. 4"
to --Figs. 4A and 4B--; and
line 9, change "the lower electrophoretogram" to --Fig. 4C--.

IN THE CLAIMS:

Claims 1 to 12, cancel without prejudice to the subject matter thereof and add the
following claims in their place:

-- 13. A labeled protein which comprises a protein portion and a labeling compound
chemically linked to a C-terminal of the protein portion,

wherein said labeling compound comprises a) an acceptor portion and b) a non-radioactive
label substance chemically linked to the acceptor portion, and said acceptor portion comprises one
member selected from the group consisting of puromycin, a puromycin derivative having the
ability to bind to the C-terminal of a synthesized protein when protein synthesis is carried out in a
cell-free protein synthesis system or in a living cell, 3'-N-aminoacylpuromycin aminonucleoside
and 3'-N-aminoacyladenine aminonucleoside.

14. The labeled protein according to claim 13, wherein said acceptor portion comprises puromycin.

15. The labeled protein according to claim 13, wherein said acceptor portion comprises a puromycin derivative.

16. The labeled portion according to claim 15, wherein said puromycin derivative is one member selected from the group consisting of ribocytidyl puromycin, deoxycytidyl puromycin and deoxyuridyl puromycin.

17. The labeled protein according to claim 13, wherein said label substance is a fluorescent dye.

18. The labeled protein according to claim 17, wherein said fluorescent dye is fluorescein.

19. The labeled protein according to claim 13, wherein said labeling compound is fluoresceinylphosphopuromycin or fluoresceinylthiophosphopuromycin.

20. A labeled protein which comprises a protein portion and a labeling compound chemically linked to a C-terminal of the protein portion,

wherein said labeling compound comprises an acceptor portion and a label substance chemically linked to the acceptor portion, and said acceptor portion comprises one member selected from the group consisting of 3'-N-aminoacylpuromycin aminonucleoside and a 3'-N-aminoacyladenosine aminonucleoside.

21. A labeling compound for labeling a protein, which comprises an acceptor portion and a non-radioactive label substance chemically linked to the acceptor portion, wherein said

acceptor portion comprises one member selected from the group consisting of puromycin, a puromycin derivative having the ability to bind to the C-terminal of a synthesized protein when protein synthesis is carried out in a cell-free protein synthesis system or in a living cell, 3'-N-aminoacylpuromycin aminonucleoside and a 3'-N-aminoacyladeniosine aminonucleoside.

22. A labeling compound for labeling a protein, which comprises an acceptor portion, said acceptor portion comprising one member selected from the group consisting of 3'-N-aminoacylpuromycin aminonucleoside and a 3'-N-aminoacyladeniosine aminonucleoside. --

IN THE DRAWINGS:

Please replace Figs. 1 to 4 presently on file with attached Figs. 1 to 3 and 4A, 4B and 4C.

REMARKS

Favorable reconsideration is respectfully requested.

The claims are 13 to 22.

The above amendment corrects minor editorial errors in the specification and presents a new set of claims which correspond to those in the response of September 29, 2000 in the parent application.

The significance of these claims will become further apparent from the remarks below.

Support for the new claims is evident from page 2, line 19 to page 11, line 10 and page 12, lines 11-21 of the present specification. Specifically, the labeling compound is described in detail on page 8, line 1 from the bottom to page 11, line 10. In particular, it is disclosed on page 9, line 5 to page 10, line 5 that the acceptor portion may comprise puromycin, a puromycin derivative having the ability to bind to the C-terminal of a synthesized protein when protein synthesis is carried out in a cell-free protein synthesis system or in a living cell, 3'-N-aminoacylpuromycin aminonucleoside (PANS-amino acid) or 3'-N-aminoacyladeniosine

aminonucleoside (AANS-amino acid). Examples of the labeling compound include Fluorpur and Fluorthiopur as described on page 12, lines 11-21. Fluorpur and Fluorthiopur represent fluoresceinylphosphopuromycin and fluoresceinylthiophosphopuromycin, respectively.

Claims 1-4 and 8 were rejected under 35 U.S.C. 112, first paragraph in the parent, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-4 and 8 were rejected under 35 U.S.C. 112, first paragraph in the parent, because the specification does not reasonably provide enablement for any labeled proteins and labeling compound.

By the above amendments to the claims, the scope of the claims is properly supported and enabled by the present specification.

In view of the above amendment, the rejection is overcome.

Claims 1-4, 6 and 8 were rejected under 35 U.S.C. 102(b) as being anticipated by Nemoto et al. (FEBS Letters, 414, 405-408 (1997)) in the parent.

This rejection is respectfully traversed.

The labeled protein and the labeling compound as claimed in new claims 20 and 22 are based on original 5 which was not been rejected in the parent. Claims 20 and 22 are thus allowable.

The present invention, as claimed in new claims 13-19 and 21, relates to a labeled protein which is a protein labeled by a non-radioactive label substance and a labeling compound comprising a non-radioactive label substance. The labeled protein of the present invention can be produced by carrying out protein synthesis in the presence of the specified labeling compound (for example, see page 13, lines 2 to 14 of the present specification).

Nemoto et al. disclose an "in vitro virus" virion, that is, a molecule in which a protein is linked to mRNA encoding the protein through a DNA spacer and a P-acceptor (page 406, right column, Fig. 1). The "in vitro virus" virion is prepared by constructing an "in vitro virus" genome, that is, a genome composed of mRNA encoding a protein, a DNA spacer, a P-acceptor

and rCpPur, and translating the mRNA region of the genome. In Nemoto et al., ³²P-labeled rCpPur is used (page 406, right column, lines 5-24; and page 407, left column, Fig. 2). The deficiencies of such are discussed, e.g. at page 1 of the present specification. However, the use of the non-radioactive label substance as presently claimed is neither disclosed nor suggested by Nemoto et al. nor is there any motivation from Nemoto et al. to produce such substance. Therefore, the labeled protein and the labeling compound as presently claimed are neither disclosed nor suggested by Nemoto et al.

In addition, Nemoto et al. relates to genotype assignment to phenotype (page 405, abstract), and the purpose of using the ³²P-labeled rCpPur is for confirmation of intermolecular bonding of rCpPur to the C-terminal end of the protein, as is clear from the fact that ³²P-labeled rCpPur is used in combination with ³⁵S-labeled methionine (page 406, right column, lines 5-24). Labeling of a protein by the protein synthesis in the presence of the presently specified non-radioactive labeling compound is not obvious from Nemoto et al. Accordingly, the labeled protein and the labeling compound as presently claimed are unobvious from Nemoto et al.

The rejection in the parent is thus untenable.

Claims 1-6 and 8 were rejected under 35 U.S.C. 102(a) in the parent as anticipated by Yanagawa et al. (WO 98/16636).

This rejection is also respectfully traversed.

The labeled protein and the labeling compound described in Yanagawa et al., which are the same as those claimed in the present application, were made by the inventors of the present application (Hiroshi Yanagawa, Naoto Nemoto and Etsuko Miyamoto). Therefore, the inventions described in Yanagawa et al. are not those of another.

In support of this fact, there is re-submitted herewith a declaration under 37 C.F.R. 1.132 from the parent.

Thus, the rejection on Yanagawa et al. is overcome.

Another declaration from the parent is also re-submitted with regard to the Yanagawa et al. reference cited in the Information Disclosure Statement of June 5, 2000 in the parent,


indicating that the reference cited therein is also the work of the present inventors and is thus unavailable as prior art.

No further issues remaining, allowance of this application is respectfully requested.

If the Examiner has any comments or proposals for expediting prosecution, please contact the undersigned at the telephone number below.

Respectfully submitted,

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